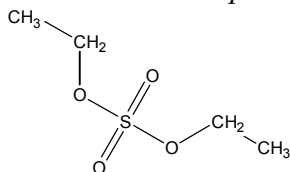


DIETHYL SULFATE

CAS No. 64-67-5

First Listed in the *Fourth Annual Report on Carcinogens*



CARCINOGENICITY

Diethyl sulfate is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC V.4, 1974; IARC S.4, 1982; IARC S.7, 1987). When administered by subcutaneous injection, diethyl sulfate induced local sarcomas in rats. Subcutaneous injection of diethyl sulfate to pregnant rats induced malignant tumors of the nervous system in their offspring. A few tumors of the forestomach occurred in rats given diethyl sulfate by gavage.

There is limited evidence for the carcinogenicity of diethyl sulfate from studies in humans (IARC S.4, 1982; IARC S.7, 1987). In a historical cohort study of process workers, chemical mechanics, and refinery workers at a factory manufacturing isopropyl alcohol and ethanol by the strong acid process, which produces high concentrations of diethyl sulfate, excess mortality from upper respiratory (laryngeal) cancer was found among process workers.

PROPERTIES

Diethyl sulfate is a colorless, moderately viscous, oily liquid that darkens with age. It has a faint ethereal odor. It is miscible with alcohol, ether, and probably most polar organic solvents. Diethyl sulfate rapidly decomposes into ethyl hydrogen sulfate and alcohol upon heating or in hot water. Diethyl sulfate is available as a technical grade that contains 99% active ingredient.

USE

The only commercial use of diethyl sulfate is as an alkylating agent to convert active hydrogen compounds, such as phenols, amines, and thiols, to their corresponding ethyl derivatives. Diethyl sulfate can be used in the preparation of a wide variety of intermediates and products in surfactants, dyes, agricultural chemicals, pharmaceuticals, and other specialty products. Because alternative ethylating agents are available commercially, it is difficult to determine which ethyl derivatives are formed from diethyl sulfate. However, the quaternary ammonium salts are formed by the alkylation of tertiary amines and are used as surfactants in detergents and fabric softeners (NCI DCE, 1985d).

PRODUCTION

Diethyl sulfate has been produced commercially in the United States for at least 50 years (IARC V.4, 1974). The 1997 *Directory of Chemical Producers* lists one company yielding an undisclosed amount of the compound (SRIa, 1997). Annual U.S. production has been estimated at 11 million lb (IARC V.54, 1992). The 1979 TSCA Inventory reported two producers of diethyl sulfate with a combined production of 6.1 million lb in 1977, and nine U.S. companies importing a total of 775,000 lb (TSCA, 1979). No data on exports were available.

EXPOSURE

The primary routes of potential human exposure to diethyl sulfate are inhalation and dermal contact. Exposure to diethyl sulfate may occur during its production and use as a chemical intermediate, primarily as an ethylating agent (NCI DCE, 1985d). It appears, however, that most exposures have been associated with its use, since domestic production of diethyl sulfate has not been widespread (IARC V.4, 1974). The potential for exposure to diethyl sulfate during its use would appear to be high since a wide variety of intermediates and products are prepared from it, but concomitant exposure to other chemicals is also likely (NCI DCE, 1985d). The National Occupational Exposure Survey (1981-1983) indicated that 2,261 total workers, including 164 women, potentially were exposed to diethyl sulfate (NIOSH, 1984). The National Occupational Hazard Survey, conducted by NIOSH from 1972 to 1974, estimated that 1,646 workers were potentially exposed to diethyl sulfate in the workplace in 1970 (NIOSH, 1976). Quantitative exposure data were not located in the available literature. This may be related to the fact that a method for measuring diethyl sulfate in air at ppm concentrations has only recently been developed (NCI DCE, 1985d).

It has been documented that workers involved in the production of ethanol by the strong acid process were frequently exposed to diethyl sulfate. Analysis of the history of an ethanol plant and interviews with present and former supervisors indicated that diethyl sulfate exposures were likely to occur when process equipment was opened for manual cleaning and from leaky pump seals. It was noted that the production equipment had to be opened frequently to clean deposits that fouled absorbers, extract soakers, and other pipes and vessels. These deposits included heavy sticky materials, such as coke or tar, which prevented complete draining or purging of unit streams that contained high concentrations of diethyl sulfate. The ethanol strong acid process workers were also exposed to sulfuric acid mist, coke, tar, heat-transfer fluid vapor, sulfur trioxide, and ethyl ether (see also Coke Oven Emissions and Soots, Tars, and Mineral Oils in Section III.A). Unfortunately, the lack of quantitative monitoring data for diethyl sulfate precludes estimation of long-term average and maximum probable average exposures. Furthermore, although diethyl sulfate is a compound that is highly irritating to the respiratory tract, eyes, and skin, information regarding vapor irritation, detection, or identification thresholds that might help establish maximum likely exposures were not located (NCI DCE, 1985d). The Toxic Chemical Release Inventory (EPA) estimated that 3,208 lb of diethyl sulfate were released to the environment, specifically to air, from 16 facilities that produced, processed, or used the chemical in the United States in 1996. One facility located in Calvert City, Kentucky, reporting under industrial classifications for manufacture of industrial organic chemicals not elsewhere classified (SIC Code 2869), cyclic crudes and intermediates (SIC Code 2865), and pharmaceutical preparations (SIC Code 2834), accounted for 65.1% of the total air release (TRI96, 1998).

REGULATIONS

EPA regulates diethyl sulfate under the Clean Air Act (CAA), Superfund Amendments and Reauthorization Act (SARA), and Toxic Substances Control Act (TSCA). The National Emission Standards for Hazardous Air Pollutants (NESHAP) addresses diethyl sulfate emissions from processing facilities under CAA. SARA sets threshold amounts for diethyl sulfate used, manufactured, or processed at a facility. TSCA requires that manufacturers and importers report general production, use, and exposure information for diethyl sulfate. EPA has proposed regulating diethyl sulfate under the hazardous waste disposal rule of the Resource Conservation and Recovery Act (RCRA). OSHA regulates diethyl sulfate under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-47.